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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/804,490	03/12/2001	Linda Burkly	C1BT-P01-114	2374

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EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	PAPER NUMBER
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/804,490	BURKLY ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,6,9,10,13-17,21-25,30,32,34 and 37-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *9,10,32 and 45* is/are allowed.

6)☒ Claim(s) *1,2,5,6,13-16,21-24,30,37-44 and 46-49* is/are rejected.

7)☒ Claim(s) *17,25 and 34* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth on 10/27/2004, have been entered in full.

Response to Amendment

Applicant is notified that any outstanding objection or rejection that is not expressly maintained in this Office action has been withdrawn. Specifically, the rejection of claims 1, 2, 5, 6, 9, 10, 13-17, 21-25, 30, 32, 34, 37-46 under 35 U.S.C. 103(a) as being unpatentable over Patent No: 6639051, Wang-EA, in view of Ericson-J et al., Cell 87(661-673)1996 and U.S. Patent No: 481656 is withdraw due to Applicant's amendment in the specification asseting that the subject matter of the instant disclosure was developed as part of a joint research agreement between Curis, Inc. (Patent No: 6639051) and Biogen, Inc., see MPEP 706.02(l). Applicant's representative further asserts that the subject matter of the present application and US Patent No: 6639051 were made by or on behalf of parties to a joint research agreement that was in effect on or before the date the claimed invention was made and that the claimed invention was made as a result of activities undertaken with in the scope of the joint research agreement. Applicants' representative further asserts that Applicants' statement and amendments, as well as the fee paid, are believed to comply with the safe harbor provisions of the CREATE Act, 37 C.F.R. 171(g)l and 37 C.F.R. 1.17(i).

New Rejections/Objections:

Specification

The disclosure is objected to because of the following informalities: there is a blank on page 21.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 5, 6, 13-16, 21-24, 30, 37, 38-44, 46-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for inhibiting the growth or differentiation of a hair follicle epithelial cell using anti-hedgehog antibody that specifically binds sonic hedgehog, humanized and fragments thereof, does not reasonably provide enablement for methods regarding other epithelial types and nor for antibodies that do not specifically bind sonic hedgehog. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

First it should be noted that the phrase "or fragments thereof" (e.g. claim 1) given its broadest reasonable interpretation when read in light of the specification is limited to those

fragments of the recited antibodies that retain the required antigen-binding specificity, see page 16 of the specification.

The specification demonstrates that anti-sonic hedgehog antibodies administered to fetal and peri-natal mice inhibit the growth of hair. Additionally, Applicant's published work demonstrates that topical administration of such antibodies to adult mice also inhibits hair growth, see Wang-LC et al., Journal of Investigative Dermatology, 114(5)901-908, 2000. Interestingly, the data indicate that epithelial cells other than those in the hair follicle were not effected. The exception being cells of the intestine when treated early in development, see line 1 of page 36 of the specification, wherein it is noted that these neonates died within the first week after birth due to massive gastro-intestinal tract defects. Assuming the affected intestine cells were epithelial, it is unclear what benefit this teaching would provide. Thus, the data indicate that the specification has taught how to inhibit hair follicle epithelial cell growth and development, and also gastro-intestinal epithelium of early fetal mice. However, the specification has not taught what use the latter method might have. Thus, the specification has not provided an enabling basis to make and use the methods as they relate to the genus of epithelial cells as claimed.

Additionally, the methods were accomplished with an antibody that specifically binds sonic hedgehog. As reviewed by Wang-LC et al., (supra), sonic hedgehog has been demonstrated to be essential for follicle development, whereas other hedgehog family members do not appear to be involved, see page 901 of Wang-LC et al. Thus it can be assumed that only antibodies that are capable of interfering with sonic hedgehog signaling would be useful in the claimed methods. The claims encompass antibodies that bind to hedgehog family members in

general. While it might be assumed that there would be some overlap in antibody binding among family members, the specification does not support the use of the genus of hedgehog binding antibodies. It is appreciated in the art that the different hedgehog family members differ significantly in amino acid sequence. It is also well appreciated in the art of antibody production that it is unpredictable which amino acids are critical antigenic determinants (see Alexander et al., Proc. Natl. Acad. Sci. 89(3352-3356)1992. Protein antigenicity can be significantly reduced by substitution of even a single residue. Further, even if an amino acid substitution does not destroy the activity of the immunizing protein, the substitution may significantly reduce the antigenicity of the protein (see the Abstract of Alexander et al.). The specification has not provided sufficient information as to which antigens can be used that bind the family of hedgehog proteins, yet are still useful for practicing the claimed method.

Therefore, due to the large quantity of experimentation required to identify epithelial tissues that are amendable to the treatment methods, other than hair follicle epithelial cells, if any can be found, and the large quantity of experimentation required to identify antigens or antibodies capable of specifically interrupting sonic hedgehog signaling but that also bind other hedgehog family members, the contrary state of the art which suggests that the effect of anti-hedgehog antibodies is limited to hair follicle epithelial cells, e.g. Wang et al. (supra), and the effect of amino acid sequence identity on antigen determination (Alexander), the lack of direction and guidance provided by the specification as to which particular epithelial cells are amendable to the claimed methods and to which antigens would produce the required antibodies, and the breadth of the claims which require all epithelial cell and/or antibodies to all hedgehog

family members, undue experimentation would be required of the skilled artisan to make and use the invention commensurate in scope to that which is claimed.

Claims 1, 2, 5, 6, 13-16, 21-24, 30, 37, 38-44, 46-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As set forth above, the claims require either the broad genus of epithelial cells or the broad genus of hedgehog-binding antibodies or both. Yet the specification has only provided a description of a useful method regarding only a single epithelial cell type, hair follicle epithelial cells, using a single type of antibody, i.e. an anti-sonic hedgehog antibody. The data in the specification and in the art would indicate that only this one type of epithelial cell would be amendable to the claimed method, i.e. presumably all of the epithelial cell-types of the developing mice would have been exposed to the antibody, yet only one type responded in a useful way.

The instant disclosure of a single species of epithelium and a single type of antibody, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence,

falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. The instant specification discloses, however, a single species of epithelium and a single type of antibody, which is not sufficient to describe the essentially limitless genera encompassed by the claims.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the disclosed methods regarding hair follicle epithelial cells and sonic hedgehog-binding antibodies, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Allowable Subject Matter

Claims 17, 25, 34 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 9, 10, 32, 45 are allowed.

Applicant remarks, 10/27/2000 are noted and made of record, however they do not appear to be germane to the new issues raised in this Office action.

Additional References of Relevance:

The following reference is deemed relevant to the instant Application but is not being relied upon as the basis for any rejection of the claims in this Office Action:

Leenal Bruckner-Tuderman, Journal of Investigative Dermatology, 114(5)pg899, 2000, reviews Applicant's published work and makes the following statement: "Treatment of the skin with antihedgehog blocking monoclonal antibodies provides a system to conditionally disrupt the hedgehog pathway. Thus, an inducible and reversible hairless phenotype can be generated that will be a valuable model for studying the regulation, mechanisms, and pharmacologic manipulation of hair regeneration".

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867. Official papers filed by fax should be directed to **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

January 18, 2007

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER